Title: A Web-Based Protocol Tracking Management System for Clinical Research

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Background

The National Institute of Neurological Disorders and Stroke (NINDS) is developing an integrated clinical informatics and management system to be used by its intramural clinical researchers. The Clinical Informatics and Management System (CIMS) is a centralized clinical data management and analysis system that will assist clinical investigators in managing protocols and research data as well as in integrating disparate data sources for analysis. An overview schematic of CIMS is depicted in Figure 1. CIMS consists the following major components: 1) A *Protocol Tracking Management System* (PTMS) that supports protocol submission, approval, and monitoring of protocol review process. 2) A *clinical study informatics system* provides patient data management via protocol setup for patient recruitment, screening, enrollment, dynamic form creation, data collection, monitoring, and reporting; 3) A *data integration* module provides data warehousing services to collect data from a variety of data sources such as external scientific databases; its scope also encompasses analytics tools that will facilitate data mining and statistical analysis of data from CIMS as well as the external sources to support biomedical discovery and translational research.

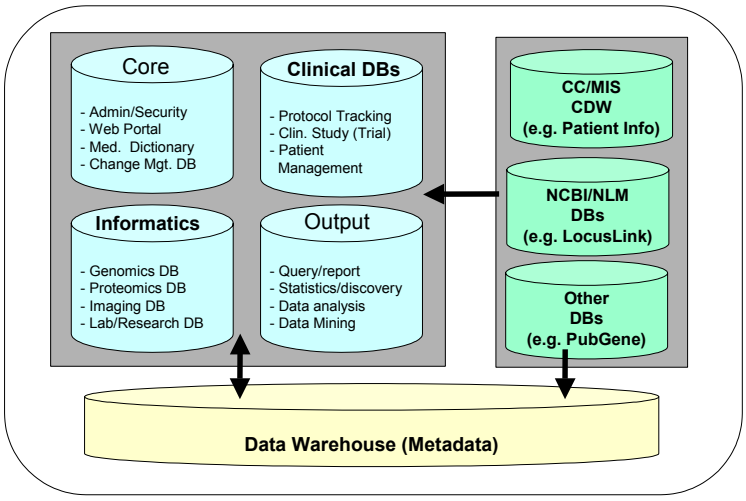

Figure 1: Clinical Informatics and Management System (CIMS) overview schematic.

Introduction

Clinical research approval processes are complex since they involve human subject welfare as well as regulatory and ethical concerns. Typically, clinical research institutions have an elaborate established review process; the labor-intensive and time-consuming nature of this process can result in approval delays thus significantly impacting the biomedical research.

PTMS is a multi-tiered, web-based information system designed to make the process of protocol approval more efficient, organized, and accurate. The system enables the *principal investigators* (PIs) to initiate, track and manage clinical studies, monitor review processes, view status changes, and quickly respond to requests for additional information. In addition, it allows the *protocol coordinators* (PCs) to manage the entire *Institutional Review Board* (IRB) approval process.

PTMS Overview

From the onset of preparing protocol submission, a PI enters her protocol information online, attaches the necessary files to the protocol, and electronically submits the protocol and attachments directly for review. The PI can print the *Clinical Research Protocol Initial Review Application* form or other

documents. Once her protocol is submitted, the PI can track the ongoing status of protocol reviews and view or respond to comments made on a protocol by a PC, a *statistical reviewer*, or an *IRB primary reviewer* regarding a concern, deficiency or stipulation. The PI can also designate authorized users to view or manage the details of the protocol.

Figure 2 shows an example workflow and status for a single protocol. The rows represent various review processes in a protocol lifecycle. The columns represent series of approval steps that a review has go through. Each cell contains a color-coded status of the review step. By clicking on the cell, investigators and reviewers can see a detailed review history and change review states.

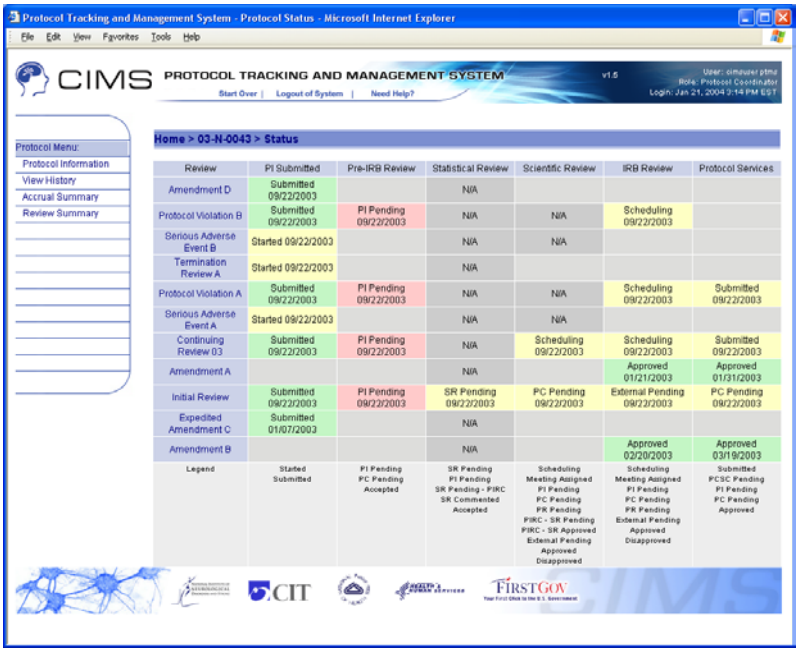

Figure 2: Protocol review workflow and current Status.

Architecture Design Framework

Since the CIMS system needs to support various client computing platforms, it has been designed as a web-based application. To support the requirements of system criticality, data sensitivity and the need to scale upward, a multi-tiered service oriented architecture (SOA) based on the J2EE platform was selected (see Figure 3). The four tiers partition the application so that each tier can be executed on separate hardware platforms. In addition, several open-source frameworks were adopted to accelerate development times, increase reliability, and improve maintainability and interoperability of the web application.

The core frameworks of the PTMS architecture include the Apache *Struts*, *Tiles*, and *Object-Relational Bridge* (OJB). Using these open-source frameworks the development proceeded quickly from prototype to full implementation with minimal additional infrastructure development. Despite continuing changes to the requirements affecting page layout and database design, the impact of these changes were minimized.

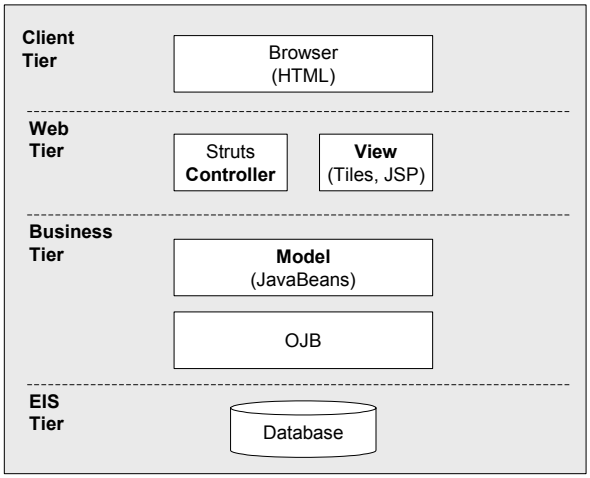

Figure 3: Multi-tiered, J2EE web application architecture.

The Struts framework drives the application. This framework contains the main Java Servlet that accepts and forwards web requests. Modification of merely one XML configuration file achieves the functionality organizing the application flow, adding new pages, and performing basic form field validations. The page layout was designed using a Struts plug-in known as Tiles, which allows each page to be broken down into sections. This design allows one template to describe the basic layout, while only sections that change need to be coded as separate Java Server Page (JSP) pages. As such, changes to the entire application page layout be done in a matter of minutes.

For the database interface, an object-relational layer called OJB was used. This layer relies on an XML file to map Java objects to relational database tables and columns. OJB also caches objects in memory to save expensive database calls for data that has already been referenced. Since OJB supports relationships as references and collections, not a single SQL statement was written in the application. This allowed the maintenance of a working application even while the database was evolving.

Summary

A clinical research system is required to monitor the review process thus facilitate the review of scientific merit of clinical studies. This necessitates a system for tracking and monitoring protocol development. PTMS is a web-based, platform-independent system with a back-end relational database management system. By automating the review process workflow, CIMS can reduce the complexity, improve communication between the investigators and reviewers, and accelerate the review process. In addition, the open source based framework and architecture allows the application to be easily adopted and modified for other research institutions with similar requirements.

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